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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 14

Application Number: 09/767,597
Filing Date: January 22, 2001
Appellant(s): JEGLA, TIMOTHY J.

Kenneth A. Weber
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 12, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

Claims 13 and 15-18 stand rejected under 35 U.S.C. § 101 for lack of a specific and substantial credible utility. Claims 13 and 15-18 also stand rejected under 35 U.S.C. § 112, first paragraph, lack of enablement due to lack of utility. Rejection of the claims 13 and 15-18 under 35 U.S.C. § 112, first paragraph, lack of written description has been reconsidered and withdrawn.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows: Rejection of the claims 13 and 15-18 under 35 U.S.C. § 112, first paragraph, lack of written description has been reconsidered and withdrawn.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 13 and 15-18 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

A substantially correct copy of appealed claims 13 and 15-18 appears on page 19 of the Appendix to the appellant's brief. The minor errors are as follows: claim 18, as originally filed, encompasses an isolated polypeptide having molecular weight between 85 kDa to about 95 kDa, not 94 kDa, as presented in the Brief and what appears to be a typographical error.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101

Claims 13 and 15-18 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the polypeptide described therein is what is termed an "orphan protein" in the art. The nucleic acid of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete

characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to a human HAC3 polypeptide of as yet undetermined function or biological significance. It is clear from the instant application that the protein described is structurally related to the voltage-gated cation channel family, specifically it is related to a family of hyperpolarization-activated channels (HAC). It is known from the literature, that these channels are involved in broad range of functions, rhythmic activity of the cells and changes in membrane potentials among them. Mouse HAC proteins have been identified and described before, and, according to the specification of the instant application

"Isolation of human HAC3 is therefore desirable, to better understand the physiology of HAC3 in humans and for the development of therapeutic and diagnostic applications to diseases related to hHAC3 in humans" (page 3, lines 13-15 of the specification, emphasis added by the Examiner). However, in the absence of knowledge of the biological significance of this specific polypeptide, there is no immediately obvious patentable use for it. 35 USC § 101 clearly states that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. The assertion to use a polypeptide of the instant invention as the object of further research "to better understand the physiology of human HAC3" clearly indicates that the instant invention was not completed as filed, and, therefore, clearly lacks utility in currently available form.

According to the instant specification, "[m]odulators of hyperpolarization-activated channel activity may be useful for treating various pacemaker dysfunctions such as familial sinus rhythm diseases, sick sinus syndrome associated with atrial fibrillation, sinus tachycardias and bradycardias as well as ventricular arryhythmias. The modulators are also useful for treating other disorders involving abnormal ion flux, e.g., memory and learning disorders, sleeping disorders, bipolar disease, schizophrenia, CNS disorders such as migraines, hearing and vision problems, seizures, and neuroprotective agents (e.g., to prevent stroke)" (page 9, lines 2-8). It is also disclosed that the instant hHAC3 when expressed in *Xenopus* oocytes demonstrates the ability to form a cation channel and to open upon hyperpolarization (page 63, lines 16-23). Thus, based on the information provided in the instant specification, one skilled in the art would reasonably conclude that the instant claimed novel Hac3 polypeptide could be a hyperpolarization-activated cation channel. However, as it is well known in the art, each cell

expresses and produces a plurality of ion channels, cation channels among them. It is also known from the literature, that cation channels are involved in a broad range of functions, such as rhythmic activity of the cells and changes in the membrane potential. Therefore, the fact that the instant hHAC3 is asserted to be a cation channel does not unequivocally lead to the conclusion that it is directly associated with dysfunctions, disorders or conditions in which cation channels are known to be involved with. The instant specification fails to provide any scientific reasoning or evidence of record, which would associate the instant polypeptide with any dysfunction or disorder. Thus, to employ the polypeptide of the instant invention in the future methods for discovering modulators of hHAC3 polypeptides to treat "diseases related to hHAC3 in humans" is not a "real world" utility because, at the time the invention was made, no "diseases related to hHAC3 in humans" were known or disclosed, and, further, because it would eventually relate to a protein for which no specific biological function is known.

Because the instant specification does not teach a specific biological activity of the protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect, one cannot prevent or treat a condition or disease as implied by the specification. To employ a polypeptide of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the claimed polypeptide then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

Claims 13 and 15-18 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

Appellant traverses the rejection of claims for lack of specific utility on the premises that the substantial and specific credible practical utility of the novel human HAC3 polypeptides as novel cation channels allegedly lies in the field of development of agonists and antagonists of the hHAC3 channels, which "are useful for, *e.g.*, the treatment of CNS disorders related to cell excitability" (page 4, last paragraph of the Brief). Beginning at page 5 of the Brief, Appellants summarize case law on the utility requirement. The essential disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility. Appellant urges that the Examiner has offered no documentary evidence or scientific basis for the conclusion that the instant HAC3 channels lack specific, substantial and credible utility (page 6 of the Brief).

However, Appellant is mischaracterizing the basis of the instant rejection. A specification can meet the legal requirements of utility and enablement for a new polypeptide as long as the specification discloses at least one credible, specific and substantial asserted utility for the new polypeptide, or a well-established utility for the claimed polypeptide would be *prima facie* obvious to the skilled artisan. A hypothetical example may serve to clarify. For example, a hypothetical specification discloses that a claimed polypeptide is expressed in lung cancer and not expressed in healthy lung tissue. The hypothetical specification does not disclose the

physiological function of the claimed polypeptide encoded. The claimed polypeptide in the hypothetical example would not be rejected under 35 U.S.C. §§ 101 and 112, first paragraph, as it has utility and is enabled as a lung cancer marker. However, such is not the fact pattern here. The instant specification discloses that the claimed polypeptides are novel hyperpolarization-activated cation channels and, "[s]ince the hyperpolarization-activated cation channels mediate cell excitability, [the] modulators [of these channels] are useful for treating conditions related to cell excitability, such as migraine and seizure" (page 6, second paragraph of the Brief). Thus, the instant specification provides the disclosure of the novel sequences identified as HAC3 that are in general associated with cellular excitability and hypothesizes that the modulation of the activity of HAC3 would be useful in treating migraine and seizure. However, there is no disclosure that the claimed polypeptides are specifically associated with migraine and seizure or any other "conditions related to cell excitability", as implied by the instant specification. Appellant further continues that because HAC3 channels are "hyperpolarization- activated cation channels widely expressed in the CNS" (page 6, last paragraph going to page 7), they are capable of modulating cell excitability. However, it was never disputed or doubted by the Examiner that the claimed novel Hac3 polypeptides could be hyperpolarization-activated cation channels. As it is well known in the art, each cell expresses and produces a number of ion channels. It is also known from the literature, that cation channels are involved in a broad range of functions, rhythmic activity of the cells and changes in membrane potentials among them. The major issue at hand is that the instant specification fails to describe the practical utility of the claimed invention. There is no evidence of the record showing that the new cloned cation channel is associated with any specific biological process, which one would wish to manipulate for a

desired clinical effect. Nor is it shown that it is associated with known compounds, specific effects or known disorders or diseases. Therefore, in the absence of knowledge of the biological significance of this specific polypeptide, there is no immediately obvious patentable use for it.

Appellant's statement that "the Examiner offers no documentary evidence or scientific basis for the conclusion [that the novel HAC3 channels lack a specific and substantial credible utility]" (page 6, first paragraph of the Brief) has been found to be unsubstantiated. The clear evidence that the novel claimed HAC3 polypeptides at the time of the invention are not associated with any physiological function, process or specific disorder is provided by the instant specification, for example. On page 1, lines 23-30, it is stated that "[c]ation channels are a diverse group of proteins that regulate the flow of cations across cellular membranes. The selectivity of a cation channel for particular cations typically varies with the valency of the cations, as well as the specificity of a given channel for a particular cation", emphasis added. Further, on page 1, last paragraph, going to page 2, it is stated that "[c]ation channels are involved in a number of physiological processes, including regulation of heartbeat, dilation of arteries, release of insulin, excitability of nerve cells, transduction of sensory stimuli, and regulation of renal electrolyte transport", emphasis added. This information is in agreement with the accepted knowledge in the art that cation channels are indeed a diverse group of channels generally associated with plurality of physiological functions. See, for example, reference article by Pape, Ann. Rev Physiol., 1996,58, pp.299-327, presented with the Declaration of Castle (Paper No. 8), stating that "[I]ntrinsic electrophysiological characteristics [of function of central nervous system] reflect the type, location, and density of voltage- and ligand-gated ion channels that regulate the flow of ionic currents across the neuronal plasma membrane and that are

controlled by a large variety of transmitter substances and intracellular messenger systems" (page 299, Introduction). Furthermore, "cell excitability" characterizes the ability of a cell to respond and react to environmental stimuli, and is considered to be one of the most basic and general biological functions of a live cell. There is no dispute that the novel HAC3 channels might be potentially involved in regulation of "cell excitability" and further be associated with the diseases related to "cell excitability". However, based on the information provided in the instant specification, one skilled in the art would not recognize HAC3 as being associated with any particular disease, including migraine or seizures, nor would one to expect that administration of an agonist or antagonist of HAC3 would have any effect on these conditions, because the instant specification presents no scientific evidence to support such assertion.

Appellant further urges to the Declaration of Dr. Neil Castle to support the statement that "a skilled artisan would believe that a HAC3 channel can modulate neuronal and therefore cell excitability" (page 7, first paragraph). The Declaration of Dr. Neil Castle under 37 CFR 1.132 filed on August 13, 2002 has been carefully considered but found to be insufficient to overcome the instant utility rejection. The Declaration further asserts the utility of HAC3 polypeptides as hyperpolarization-gated cation channels "in promoting neuronal excitability" and proposes that they could be, therefore, be useful "for the treatment of diseases of hyperexcitability, such as epilepsy and migraine" (see page 3, sections 7 and 8 of the Declaration). However, the Declaration, as well as the instant specification, fails to clearly identify the specific connection between HAC3 polypeptides and migraine or epilepsy. One skilled in the art readily understands that hyperpolarization-gated cation channels could certainly be involved in modulation of cellular excitability. It is also clear that hyperpolarization-gated cation channels could be

associated with etiology or development of migraine and epilepsy. However, in the absence of clear understanding of the nexus between the novel HAC3 channels and a specific disorder, such as migraine or epilepsy, one skilled in the art would not know how to use the claimed sequences. Moreover, a skilled practitioner would not reasonably expect that administration of potential modulators of HAC3 would have any effect on any of the "diseases of hyperexcitability". 35 USC § 101 clearly states that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. The fact that some experimentation is required to establish if blockers of the HAC3 would decrease CNS activity as implied in the instant specification ("blockers of NAC3 channels can be expected to decrease CNS activity", see page 7, second paragraph of the Brief) simply confirms that the instant invention was not completed as filed, and, therefore, clearly lacks utility in currently available form.

Appellant further submits that "[a]ntagonists of HAC3 ion channels, therefore, have utility for (1) decreasing CNS activity, (2) modulating cell excitability, and (3) treating diseases of hyperexcitability, such as epilepsy and migraine" (page 7, last paragraph going to page 8 of the Brief). This argument has been fully answered before. Briefly, in the absence of clear nexus between HAC3 and a specific disease or disorder, "decreasing CNS activity and modulating cell excitability" clearly stands for a general assertion of an unknown specific utility. There is no dispute regarding the ability of one skilled in the art to identify agonists and antagonists of the novel claimed HAC3 based on the information provided in the instant specification (page 8, second paragraph). The major disagreement with the Appellant's position remains, however, that a skilled artisan would not know how to use these agonists/antagonists because the instant

specification provides no evidence or sound scientific reasoning to expect that, for example, administration of these agonists/antagonists would have any effect on any particular disease, including epilepsy or migraine.

At page 9 of the Brief, Appellant asserts a specific utility for HAC3 molecules as "HAC3 channels can mediate cell excitability in the CNS, which is clearly specific for the claimed HAC3 channels and not any ion channels". This statement appears to contradict the fundamental knowledge in modern electrophysiology as well as the information provided in the instant specification. It is well known in the art that each cell contains a plurality of ion channels, known and yet to be discovered, which can mediate cell excitability (see pages 1-3 of the instant specification, for example) and HAC3, based on their electrophysiological characteristics, appears to be one of them.

Appellant submits that substantial utility of HAC3 is defined as "a real-world use in the modulation of cell excitability, as well as identification of agonists or antagonists of HAC3 channels [...] useful as therapeutical agents for treating diseases related to cell excitability, such as migraine or epilepsy" (page 10, first paragraph of the Brief). This argument was fully answered before. Briefly, the protein of the instant invention belongs to a family of compounds generally related to the most general physiological mechanism, such as cellular excitability. The utility of those members of the hyperpolarization-activated ion channels family to which the claimed protein in the instant application appears to belong lies in the knowledge that they modulate a specific physiological activity in response to a specific signal. Since the instant specification does not disclose the identity of the signal or a specific physiological pathway in the connection with any process which one would wish to manipulate for a desired clinical

effect, screening for agonists or antagonists of the pathway through which that ion channel transduces its signal in response to that signal is not particularly useful.

At page 10 of the Brief, Appellant asserts a credible utility as that "one skilled in the art, after reading this application, would (a) know how to identify HAC3 channels (b) know how to identify agonists or antagonists of HAC3 channels (c) know how to use these agonists or antagonists so identified to modulate cell excitability". These arguments have not been found to be persuasive for the following reasons. One skilled in the art would not reasonably believe or find it credible that administration of modulators of HAC3 polypeptides would have an effect or make a difference in treatment of such a broad range of unrelated disorders as "various pacemaker dysfunctions such as familial sinus rhythm diseases, sick sinus syndrome associated with atrial fibrillation, sinus tachycardias and bradycardias as well as ventricular arryhythmias. [...] [M]emory and learning disorders, sleeping disorders, bipolar disease, schizophrenia, CNS disorders such as migraines, hearing and vision problems, seizures, and neuroprotective agents (e.g., to prevent stroke)" (page 9 of the instant specification, lines 2-8). Moreover, the instant specification fails to provide any evidence or sound scientific reasoning that hyperpolarized activated cation channel Hac3 is specifically associated with all these diseases and conditions. It would require making significant inventive contribution for one skilled in the art to discover which one of the disease or conditions stated in the instant specification could be treated by administration of agonist or antagonist of Hac3 polypeptide. Therefore, one would reasonably conclude that at the time the invention was made, no specific and credible utility for the claimed Hac3 polypeptides was disclosed.

Appellant's analysis of Example 8 of the Revised Interim Utility Guidelines Training Materials and comparison to the present application has been carefully review but is not deemed to be persuasive. In Example 8, a compound A, that inhibits an enzyme XYZ, to treat diseases caused or exacerbated by enzyme XYZ, has been found to have a utility because enzymes have a well established utility in the art. However, this appears to be not the factual situation here. Each enzyme has a substrate specificity, which defines its unique biological function; therefore, an inhibitor of a specific enzyme obviously would have a specific and substantial credible utility. In the instant case, "[t]he present specification states that HAC3 channels are likely to be involved in modulating cell excitability in the CNS" (page 12, last paragraph of the Brief). "Modulating cell excitability in the CNS" or "modulating the passage of ions according to various conditions" (page 13, first paragraph) does not stand for a specific condition but rather corresponds to one of the most universal biological characteristics of a live cell, thus, presenting an invitation to use a polypeptide of the instant invention as an object of further research, which, as it has been determined by the courts, alone does not support patentability. The proper analysis of the instant claims, which are drawn to an isolated polypeptide of yet undetermined significance, should be made in light of Example 12 of those guidelines, which explains why an isolated nucleic acid encoding an "orphan receptor" lacks utility in the absence of the disclosure of a specific role for either the nucleic acid or protein in a known disease or disorder or a physiological process which one would wish to manipulate for clinical effect. While not required by any statute or rule, if Appellants had disclosed a biological role or function of the claimed polypeptides, such might support a disclosed utility, such as for diagnosis or treatment of disease. However, no such role has been disclosed. This alone is not probative of lack of utility under 35 U.S.C. § 101, but is

merely one of the analyses, which must be made. If there were another specific, substantial and credible utility disclosed for the claimed HAC3, that would, in the absence of any knowledge of the biological function or role of the claimed polypeptides, be sufficient to establish utility.

Appellant's reliance on *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881 (CCPA 1980) is not found to be persuasive (pages 13-14 of the Brief). In *Nelson v. Bowler* the court reversed a finding by the Office that the applicant had not set forth a "practical" utility under 35 U.S.C. 101, and stated: "Practical utility is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public". In the instant case, assertions that "[b]ecause abnormal ion influx and altered cell excitability cause various diseases and disorders, compounds capable of modulating ion channels, such a s hyperpolarization-activated ion channels, are useful as therapeutic agents for treating these conditions" (page 14, first paragraph of the brief) clearly establish that the instant invention cannot be used "in a manner which provides some immediate benefit to the public". To grant Applicant a patent encompassing an isolated naturally occurring human protein, which is not readily usable in it's current form, would be to grant Applicant a monopoly "the metes and bounds" of which "are not capable of precise delineation". That monopoly "may engross a vast, unknown, and perhaps unknowable area" and "confer power to block off whole areas of scientific development, without compensating benefit to the public" (*Brenner v. Manson, Ibid*). To grant Applicant a patent on the claimed polypeptide based solely upon an assertion that the protein can be employed for screening agonists or antagonists to modulate cell excitability to treat various diseases and

disorders is clearly prohibited by this judicial precedent since the compensation to the public is not commensurate with the monopoly granted.

Therefore, for reasons set forth above, Appellants arguments have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility and failure to enable due to lack of utility and it is believed that the rejections should be sustained.

Respectfully submitted,

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September 5, 2003

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Respectfully submitted,

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